Secondary Polycythaemia as an Unusual Cause of Falsely Elevated Prothrombin Time and International Normalized Ratio
Vaidya N,¹ Jaisy D,¹ Koju S²

¹Department of Internal Medicine, ²Department of Haematology, Dhulikhel Hospital, Kathmandu University Hospital, Kathmandu University School of Medical Sciences, Dhulikhel, Kavre, Nepal.

ABSTRACT
Elevated Prothrombin time is common in conditions such as liver dysfunction and use of Vitamin K antagonists. Polycythaemia is among the uncommon causes of elevated prothrombin time. Elevated hematocrit greater than 55% leads to a decrease in plasma of the blood sample, thereby reducing the coagulating factors available. Hence, it is recommended to adjust the citrate (anticoagulant) concentration for collecting blood sample from patients with high Hematocrit to get correct Hematocrit value.

KEY WORDS
Hematocrit, Polycythaemia, Prothrombin time

INTRODUCTION
Liver dysfunction, use of Vitamin K antagonist and Disseminated Intravascular Coagulation (DIC) are the recognised causes of elevated Prothrombin Time and International Normalized Ratio (PT-INR). There are other uncommon causes of this elevation.¹ We present a case where PT-INR is falsely elevated due to secondary polycythaemia.

CASE REPORT
A 48 years old gentleman with known case of Hypertension, Dyslipidaemia, Metabolic Syndrome and Obstructive Sleep Apnoea Syndrome (OSAS) presented to Medicine OPD of Dhulikhel Hospital with headache and facial flushing. He is a regular smoker and consumes alcohol infrequently. On examination, he was metabolically obese with Body Mass Index (BMI) of 36.2. He was polycythaemic. Rest of the physical findings were normal. Routine blood evaluation showed Haemoglobin 22.5 gm/dL, Hematocrit 71 %, PT 55 seconds, INR 4.2 (ISI: 1.0 Control value for PT:12 Sec), Activated partial thromboplastin time (APTT) 36 sec (Normal range: 22-26). He had not taken drugs like Warfarin and liver function test was normal. There was no apparent history of bleeding. He was then admitted for evaluation of coagulopathy. Other investigations including chest X-ray and ECG were normal. Echocardiography showed Diastolic Dysfunction. Test for JAK2 V617F mutation was sent to rule out Polycythaemia Vera, which was absent. For the unrecognized cause of elevated PT, the sample was later citrate corrected and the report was normal with PT of 16 seconds and INR 1.2.
Final Diagnosis was made as “Falsely elevated PT INR due to secondary polycythaemia due to OSAS”. Twice weekly Phlebotomy was planned. The patient was advised for arranging CPAP for OSAS along with lifestyle modifications. On follow up, his symptoms are improving.

**DISCUSSION**

Increased PT-INR is frequently encountered in daily practise. The two most common causes of raised PT-INR are liver dysfunction and use of Vitamin K antagonists. Other common causes are DIC, Vitamin K deficiency and APLA Syndrome. Polycythaemia is characterized by an increase in number of red blood cells and/or the amount of haemoglobin (Hb) per unit volume of blood. The most appropriate haematological parameter for assessment is the Hematocrit (Hct). Secondary polycythaemia is characterized by increased erythropoietin. OSAS is characterized by intermittent hypoxia and is one of the numerous causes of secondary polycythaemia.

Elevated Hematocrit greater than 55% leads to a decrease in plasma component of the blood sample, thereby reducing the coagulating factors available. In normal conditions, the proportion of anticoagulant (Citrate) to blood in collected vial is 1:9. In blood sample with high Hematocrit value, the citrate concentration is increased in plasma fraction of collected tube. This cause a false elevation of clotting time in coagulation profile. This blood sample with high Hematocrit (> 55%) is needed to adjust the final citrate concentration for correct value of routine coagulation test maintaining the ratio of anticoagulant and plasma to 1:9 which will prevent from reporting falsely elevated coagulation testing value. This study aims to compare the effect of high Hematocrit in citrate adjusted and non-citrate adjusted concentration in routine coagulation testing result.

Blood sample was drawn in light blue capped 3 ml vacutainer containing 3.2% sodium citrate as anticoagulant. PT and APTT tests were done for initial investigation in coagulation test and both PT and APTT was found to be elevated in sample with the value of 55 seconds and 36 seconds respectively. Initially Hematocrit value was ignored for coagulation investigation but later when coagulation testing value was reported spuriously high without any clinical significance, high Hematocrit of 71% was noted in patient and suspect for false reporting due to elevated Hematocrit. Then after getting informed consent, two blood samples for citrate adjustment and non-citrate adjusted were drawn for investigation of coagulation testing. For non-citrate adjustment, blood sample was directly drawn in non-citrate adjusted vacutainer tube while for citrate adjusted sample, concentration of citrate is corrected based on Hematocrit value according to Clinical and Laboratory Standard Institute (CLSI) guideline.

To calculate the amount of citrate remain in the blood drawing tube, we use the following formula

$$C = \frac{(1.85 \times 10^{-3})(100 – \text{Hct})(V_{\text{blood}})}{7.8}$$

where, C is the volume of citrate remaining in the tube, Hct is the Hematocrit of the patient, and V is the volume of blood to be added. (If a 3 ml tube is used, the volume is 2.7 ml) and 1.85 x 10^-3 is constant (taking into account the citrate volume, blood volume and citrate concentration). PT and APTT value for non-citrate adjustment sample is 64 seconds (INR: 5.3) and 36 seconds respectively while citrate adjustment sample reported 16 seconds (INR:1.3) for PT and 25 seconds for APTT. Coagulation value for citrate adjusted and non-citrate adjusted sample were significantly different.

Many pre-analytical variables affect the result of routine coagulation assay and high value is one such variable that changes the coagulation testing value. Hence, it is recommended to adjust the citrate (anticoagulant) concentration for collecting blood sample from patients with high Hematocrit (> 55%). Failure to adjust ratio of anticoagulant to blood sample leads to false elevation of coagulation testing value.

**REFERENCES**